REMARKS

Applicants maintain the rejection of claims 1–4 and 7–11 under 35 U.S.C. § 103 based on Salituro et al. (US 6,093,742) is based upon improper hindsight. When the disclosure of Salituro et al. is considered as a whole, it does not provide any direction to substitute the phenyl groups of compound 20 of the reference. Applicants maintain that such substitution is knowledge gleaned from their disclosure. The broad ambiguous disclosure of Salituro et al. can only be interpreted to suggest the compounds of Formula I herein have p38 activity if reference is made to applicants' disclosure.

The Office Action refers to the disclosure at column 2, lines 1–40 of Salituro et al. It is alleged that Salituro et al. teach and thus suggest that the aromatic rings may be optionally substituted with substituents such as $CON(R^3)_2$, COR^3 or SO_2NR^3. However, these teachings are limited to the aromatic rings bound directly to the urea group. Such teachings appear in the definitions for "W" and "Z," which read

> "W is a saturated, partially saturated or aromatic monocyclic or bicyclic ring system containing 0–4 heteroatoms selected from N, O, and S, wherein W optionally comprises up to 4 substituents independently selected from R^1 and R^4."
>
> Z is selected from C_3-C_7 -cycloalkyl, C_5-C_7-cycloalkenyl or aromatic or non-aromatic 5-7 membered monocyclic or bicyclic ring containing 0-4 heteroatoms selected from N, O and S, wherein Z optionally comprises up to 4 substituents independently selected from R^1 and R^4.

This language does not teach or suggest substituting the aromatic rings remote from the urea group. The teachings regarding the substitution of "W" and "Z" are supported by the detailed disclosure and examples, which include compounds where an aryl group bound directly to the urea is substituted. These teachings are also consistent with the scope of the independent and dependent claims. In contrast, the detailed description, exemplified

compounds and claims are not consistent with providing substituents on the phenyl groups of compound 20 of the reference.

The broad language at column 2, lines 34–40 does define compounds with a bridged cyclic structure (where R^1 is OR^3, $N(R^3)_2$, CO_2R^3, $CON(R^3)_2$, COR^3, $NHCOR^3$, SO_2NR^3 or SR^3 and R^3 is C_{6-20} aryl) but there is no clear direction to substitute the C_{6-20} aryl group. The language at column 2, lines 1–40 further indicates that "R^3 optionally contains up to four substituents selected from...,". However, these substituents are clearly not suitable for all of the R^3 moieties since R^3 includes hydrogen.

To obtain clarification of this ambiguous broad general language, one skilled in the art would need to refer to other portions of the specification and there is no direction in the specification to substitute the remote C_{6-20} aryl groups. In that the specification provides no further details with respect to substituting the remote C_{6-20} aryl groups and none are illustrated, when considered as a whole, one skilled in the art would not be motivated to employ the compounds of formula I herein to treat conditions mediated by p38. There is no basis for concluding that one of ordinary skill in the art would have reason to believe the C_{6-20} aryl substitutions do not alter a compounds p38 inhibitory activity. Other than a retrospective interpretation of the broad and ambiguous language referring to substituents on "R^3," the reference provides no other disclosure which hints or suggests the remote aryl groups can be substituted. More significantly, the disclosure of Salituro provides no indication what effects substituents on a remote phenyl group would have on activity.

The compounds identified as preferred by Salituro also provide no indication that substitution of the remote aryl ring is suitable. Compound Nos. 3, 4, 6, 12, 13, 24, 33, 61, 64, 105 and 107 are said to be "more preferred" and not one has a remote C_{6-20} aryl group. Of the 19 preferred compounds identified at column 38, lines 42–44, only compound 22 has a

remote phenyl ring. This remote phenyl ring is unsubstituted, yet there are multiple substituents on a phenyl ring which neighbors the urea group. This disclosure would not motivate one skilled in the art to add substituents to the remote C_{6-20} aryl group.

In the absence of any data or discussion with respect to substituting the remote phenyl ring let alone selecting the substituents SO_2R_x, $C(O)R_x$ and $C(NR_y)R_z$, the teachings of Salituro et al. clearly do not render the methods claimed herein obvious and the rejection under 35 U.S.C. § 103 should be withdrawn.

If there are any remaining issues which can be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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